action of BK (10-1000 ng).

However, clotrimazole (1 μM), an inhibitor of P450 reduced responses up to 80% while 7-ethoxyresorufin, another P450 inhibitor, was less effective (40% inhibition). 17-ODYA (2 μM), an inhibitor of P450 fatty acid metabolism, also reduced responses to BK (up to 50%) suggesting a role of AA. None of the inhibitors affected responses to the reference vasodilator, nitroprusside (NP,1000 ng). Vasodilator responses to BK, but not NP, were markedly reduced by 10mM TEA (85%) and procaine (80%) suggesting an effect mediated by increased K^+ conductance. Nifedipine (5 nM) almost abolished responses to BK and cromakalim (1-10 μg) but did not affect those to NP. Inhibition of ATP-sensitive K^+ channels with glibenclamide (10 μM) reduced responses to cromakalim but not those to BK. These results suggest that the coronary vasodilator response to BK is mediated by a P450-AA metabolite that stimulates a Ca^{2+}-activated K^+ channel.

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CALPONIN PHOSPHORYLATION AND VASCULAR SMOOTH MUSCLE CONTRACTION

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In response to many agonists, both inositol(1,4,5)-triphosphate (InsP3) and diacylglycerol (DAG) are formed by the hydrolysis of an inositol lipid precursor stored in the plasma membrane of smooth muscle. The InsP3 released into the cytoplasm mobilizes calcium from internal stores, whereas DAG stimulates protein kinase C. Calponin is a thin filament-associated smooth muscle protein that has been implicated to play a role in the regulation of smooth muscle [1]. Recently, we found that smooth muscle calponin is an excellent substrate for protein kinase C and the phosphorylation reduced the binding of calponin to F-actin and tropomyosin [2-4]. We have identified an important phosphorylation site in calponin by protein kinase C and demonstrated the calponin phosphorylation response following stimulation by endothelin-1 or phorbol 12,13-dibutyrate (PDBu) in 32P-labeled porcine coronary artery [5]. We found that Thr184 is the preferred site of phosphorylation and is functionally the most important of the sites phosphorylated by protein kinase C in smooth muscle calponin. We investigated the calponin phosphorylation during endothelin-1 or PDBu stimulation of intact strips of porcine coronary artery. Stimulation by endothelin-1 or PDBu resulted in a significant increase of 32P incorporation into the calponin in association with development of force. These results suggest that calponin phosphorylation plays a potential role in the regulation of smooth muscle contraction by endothelin-1 or PDBu.

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INTERACTION OF NITROXIDERGIC NERVE WITH CHOLINERGIC AND NORADRENERGIC NERVES IN BLOOD VESSEL

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Nitroxidergic nerve in dog middle cerebral arteries originates from the pterygopalatine ganglion. VIPergic and cholinergic nerve cells and fibres are histochemically detected in the rat pterygoplatine ganglion which supplies nerve fibres to cerebral arteries. Nitroxidergic, cholinergic and VIPergic nerves are expected to be originated from the ganglion. Thus, we investigated functional the interrelationship between these nerves in isolated bovine basilar arteries. Transmural electrical stimulation (TES) relaxed the arteries. The response was not reduced in the VIP- and CGRP-tolerant arteries. Evidence for a mediation by NO of the response was obtained. The relaxation was reduced by acetylcholine or physostigmine and potentiated by atropine. VIP did not alter the response to TES. It is concluded that acetylcholine from cholinergic nerves appears to act on prejunctional muscarinic receptors and decrease the synthesis or release of NO in the nerve. VIP cannot be a transmitter nor a modulator of nitroxidergic nerve functions. In dog mesenteric arteries treated with α-adrenoceptor blocker, TES produced relaxation, which was proved to be mediated by NO. Treatment with EDRF or NO synthase inhibitors did not alter the release of norepinephrine by TES. These findings suggest that NO derived from the nerve does not interfere with the amine release from noradrenergic nerves.

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